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DARBY & DARBY P.C.
805 Third Avenue
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212-527-7700

File No: 1527/0E847-US0

Date: November 24, 1999

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

Enclosed please find an application for United States patent as identified below:

Inventor/s (name ALL inventors): Arthur ASHMAN

Title: SOFT TISSUE SUBSTITUTE AND METHOD OF SOFT TISSUE REFORMATION

including the items indicated:

i. Specification and 49 claims: 2 indep.; 47 dep.; 0 multiple dep.

ii. [X] Executed Declaration and power of attorney

iii. [] Formal drawings, _ sheet (Fig.)
[X] Informal drawings, two (2) sheets (Figs. 1-3)

iv. [] Assignment for recording to:

v. [X] Verified Statement Claiming Small Entity Status

vi. [X] Check in the amount of $641.00, ($641.00 filing; $ recording) (See attached Fee Computation Sheet)

vii. [] Preliminary Amendment.

8. [] Please amend the description by inserting the following paragraph after the line containing the title on page 1: "This patent application claims the priority of U.S. provisional patent application No. 60/_____, which is incorporated herein by reference."

Priority is claimed for this application, corresponding application/s having been filed as follows:

Country:
Number:
Date:

The priority documents [] are enclosed
[] will follow.

Respectfully submitted,

Kevin L. Reiner
Reg. No. 43,040
Attorney for Applicant(s)

(D&DForms/PTO-1)

PATENT FEE COMPUTATION SHEET

	No. of Claims Presented	Extra Claims Previously Paid For	Number of Extra Claims	Rate
Basic Fee				$760.00
Design Application				$0.00
Plant Application				$0.00
Total Claims	49 - 20	- =	29 x $18.00	$522.00
Independent Claims	2 - 3	- =	0 x $78.00	$.00
Multiple Dependent Claims		x- if so, add	$260.00	$.00
Surcharge for late submission of filing fee and/or declaration ($130.00)				$
SUBTOTAL				$1,282.00
[X] Small Entity REDUCTION (Half of Subtotal)				$641.00
Fee for recordation of assignment ($40.00)				$
Charge for filing non-English language application ($130.00)				$
TOTAL				$641.00

M:\1527\0E847\CJS6675 WPD

Docket No.: 1527/0E847

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Dr. Arthur Ashman

Serial No: To Be Assigned Filed: Concurrently Herewith

For: SOFT TISSUE SUBSTITUTE AND METHOD OF SOFT TISSUE REFORMATION

VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS INDEPENDENT INVENTOR

As a below named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees to the Patent and Trademark Office with regard to the invention entitled SOFT TISSUE SUBSTITUTE AND METHOD OF SOFT TISSUE REFORMATION as described in:

[X] the specification filed herewith.
[] application serial no. filed
[] patent no. issued

I have not assigned, granted, conveyed or licensed and am under no obligation under contract or law to assign, grant, convey or license, any rights in the invention to any person who could not be classified as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

[X] no such person, concern, or organization
[] persons, concerns or organizations listed below*

*NOTE: *Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27).*

FULL NAME:
ADDRESS:

[] INDIVIDUAL [] SMALL BUSINESS CONCERN [] NONPROFIT ORGANIZATION

FULL NAME:
ADDRESS:

[] INDIVIDUAL [] SMALL BUSINESS CONCERN [] NONPROFIT ORGANIZATION

FULL NAME:
ADDRESS:

[] INDIVIDUAL [] SMALL BUSINESS CONCERN [] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Name of inventor 1: Dr. Arthur Ashman

Signature of Inventor

Date: 11/22/99

CERTIFICATE OF MAILING

I hereby certify that this paper and every paper referred to therein as being enclosed is being deposited with the U.S. Postal Service as first class mail, postage prepaid, in an envelope addressed to: Commissioner of Patents & Trademarks, Washington, DC 20231, on _____(Date of Deposit)

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Name (Print) Signature

Docket # 1527/OE847

SOFT TISSUE SUBSTITUTE AND METHOD OF SOFT TISSUE REFORMATION

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to reformation of soft tissues within the body. More particularly, the invention relates to compositions useful in reforming the shape of soft tissues and methods of using such compositions in reforming soft tissues.

2. Description of Related Art

The medical community for many years has been attempting to develop materials and techniques to replace tissues with the body. It may be desirable to replace such tissue due to, for example, injury, disease, side effects of medical procedures and surgeries, and the aging process, for example. In addition, some patients may desire to alter their appearance for cosmetic reasons, particularly the contour of visible soft tissues. Much attention has been given to the reformation of soft tissue to locally increase its volume and change its shape.

To this end, numerous replacement materials have been tried, with certain advantages and

disadvantages. Silicone has been used for decades, but can displace and harden over time. Plastic and metal implants have also been used. However, implants such as these may not have a "natural" look or feel, especially as the body changes over time.

Since the early 1980's, injectable collagen has been extensively used in various procedures. Injectable collagen is either synthetic or natural, which is derived from reconstituted bovine collagen. Injectable collagen has been used throughout the body tissues. It may be accurately controlled in both placement and amount, and may have a more "natural" look and feel than other tissue substitutes.

The primary drawback of injectable collagen is its resorbable nature. Collagen quickly undergoes proteolytic degradation within the body, resulting in relatively short clinical effectiveness. Patients must receive additional injections to maintain tissue reformation, usually at an interval of about every few months. Continual submission to the injection procedure causes the patient inconvenience, expense, and perhaps pain, discomfort, and other side effects. As with any invasive medical procedure, injection carries with it the risk of cross-contamination and infection. Moreover, as the collagen is resorbed by the body, the patient may suffer a return of the physical dysfunction the injection corrected, or experience undesirable and irregular changes in cosmetic appearance.

More recently, concern has arisen in the medical and veterinary communities regarding the transmission of tissue-born diseases among animal species and humans. For example, bovine spongiform encephalopathy may move from animals to humans and cause new variant Creutzfeld-Jacob disease, which is fatal. Accordingly, some medical experts have searched for

synthetic alternatives that reduce the use of animal-based tissues.

U.S. Patent No. 4,536,158 issued to Bruins and Ashman discloses a synthetic porous implantable bony tissue replacement. A prosthesis is formed by bonding together a material composed of polymeric particles.

U.S. Patent Nos. 4,535,485 and 4,547,390, issued to Ashman et al., disclose a synthetic material and method for making hard tissue replacement prostheses. That material is comprised of polymeric particles coated with a hydrophilic polymeric material. The particles are of sufficient size to be packed into hard tissue areas of the body, and have pores between the particles of sufficient size for tissue, i.e., hard tissue, to grow into the pores and secure the prostheses.

U.S. Patent No. 4,728,570 issued to Ashman et al. also discloses a hard tissue prosthesis material. That material comprises polymeric particles coated with a hydrophilic polymeric material, with calcium hydroxide distributed on the surfaces and within the material to induce hard tissue growth into the pores between the particles. The particles may be bonded together to form an implantable prosthesis or may be used as a packing material for forming a hard tissue prosthesis in vivo. The material is sold by Bioplant, Inc. of South Norwalk, Connecticut, under the trade name Bioplant® HTR®.

In U.S. Patent Nos. 4,902,511 and 4,912,141 issued to Kronman, an implant for fibrous or cartilaginous tissue is disclosed. A sponge-like implant is formed by polymerizing a hydrophilic polymeric material. The implant is shaped by either polymerizing it in a mold or shaping it by cutting or grinding.

While several tissue substitute materials for bony, cartilaginous, and fibrous tissues exist, it would be desirable to have substitute materials for soft tissues. It would also be desirable to have a soft tissue replacement material that was non-resorbable, supple, flexible, and durable so that a patient would not have to undergo repeated procedures. Also, a replacement material that could be implanted in loose (particulate) form for in vivo integration that did not migrate would be highly desirable.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide a soft tissue substitute.

It is another object of the invention to provide a soft tissue substitute that is at least partially non-resorbable, supple, flexible and durable so that patients do not need to undergo repeated procedures.

Another object of the invention is to minimize patient discomfort, risk of infection and side effects of repeated medical procedures.

It is another object of this invention to provide a soft tissue substitute that may be implanted into the body in loose (particulate) form, that does not migrate.

It is a further object of this invention to provide a soft tissue substitute that is synthetic, bioinert and may contain natural materials.

It is yet another object of the invention to provide a soft tissue substitute that may be used to reform and augment soft tissues, including soft tissue contour defects.

The present invention is a soft tissue implant material comprising biologically-compatible

polymeric particles. The particles may have a porous surface. The particulate nature of the material provides a natural feel and is held by the body's existing tissue and tissue formed into the pores and around and between the particles. The implant material may be combined with a variety of matrix materials, including collagen. The volumetric ratio of particles to matrix material may be varied depending on the application, i.e. the soft tissue intended to be replaced. The particles may compose up to 100% of the volume of the material. The implant material may also contain bioactive substances, which may, for example, be grafted to the particles. The implant material may be formed by known methods.

The invention also features methods for reforming and augmenting soft tissues. The implant material may be implanted into soft tissue at a desired location. In injectable form it may be accurately placed within soft tissue using a syringe or orthoscopic device. In this manner, the implant material may be used to correct soft tissue defects, (e.g. by plumping and expanding tissues) remediate medical conditions such as incontinence, and for cosmetic procedures.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other features of the present invention will be more readily apparent from the following detailed description and drawings of an illustrative embodiment of the invention where like reference numbers refer to similar elements throughout the several view and in which:

FIG. 1 shows a cross-sectional schematic of cutaneous soft tissue having a contour

defect;

FIG. 2 shows a cross-sectional schematic of the cutaneous tissue of **FIG. 1** after the implant material of the present invention has been implanted subcutaneously; and

FIG. 3 shows a schematic of a portion of the human male urinary tract after prostrate removal with constriction of the urethra after the implant material of the present invention has been injected into the sphincter urethrae.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention features materials that may be implanted into soft body tissue for correction of soft tissue defects or for soft tissue augmentation. The material comprises biologically-compatible polymeric particles, which have intraparticulate pores. The material may be combined with collagen or other matrix materials including, but not limited to, blood, saline, sterile water or glucose. The matrix material acts as a medium for particles and may help in the dispensing, e.g., injection, of the material when first implanted. The use of matrix materials also allows the amount of soft tissue augmentation to be more accurately controlled. As matrix material is resorbed, additional implantation can be accomplished, as necessary. The volume of matrix material in the implant material is preferably between about 30% and 65%. Most preferably, the volume of is about 50%. However, one skilled in the art will appreciate how much matrix material to combine to obtain a particular desired result.

A combination of the particulate material and collagen has several advantages. First, collagen has a known consistency. Second, collagen is resorbable by the body, and is completely

resorbed over a period of a few months. Synthetic particles are not resorbed, and may be permanently retained bioinertly within the tissue. Collagen has a natural look and feel when injected for cosmetic applications, helping ensure the patient is satisfied with the outcome. Porous synthetic particles offer a similar outcome.

In another embodiment of the invention, the implant material may be combined with adipose (fat) tissue. Fat tissue acts as a bulking agent that helps to dispense and hold the implant material in place after implantation. Fat is also resorbable by the body, and when taken from the patient's own body, the risk of rejection of is significantly reduced. As discussed herein, other embodiments of the invention may utilize matrix materials to facilitate delivery of the material to the implantation site.

In a further embodiment of the invention, the implant material may contain bioactive substances. These substances can be therapeutic and, for example, promote tissue growth, i.e., growth factors, or act as an antimicrobial. These substances may also be grafted to or absorbed by the particles, and may be of a nature so that they are time-released in the surrounding tissue. Those skilled in the art will recognize the various bioactive substances that may be incorporated into the implant material and their medical value, depending on the application.

Preferably, the polymeric particles have an hollow inner core, and an outer layer of a different, hydrophilic polymeric material such as polymeric hydroxyethylmethacrylate (PHEMA), which preferably is comprised of a copolymer of monomeric hydroxyethylmethacrylate and a cross-linking agent. Preferred cross-linking agents include triethyleneglycol dimethacrylate, tetraethyleneglycol dimethacrylate, diethyleneglycol

dimethacrylate, and monoethyleneglycol dimethacrylate. Cross-linking agents preferably comprise from about 0.1 percent to about 5 percent by weight of monomeric hydroyethylmethacrylate. The inner core is preferably an acrylic polymer, such as polymethylmethacrylate (PMMA). In another embodiment of the invention, calcium hydroxide coats the outer layer. Calcium hydroxide has an alkaline effect that may reduce acidic environments that have been associated with infection. Suitable material includes various formulation of Bioplant® HTR® available from Bioplant, Inc.

When this material is implanted into soft tissue, dense, fibrous and flexible tissue forms around and into the porous portion of the material. This occurs within a few days of implantation. The implanted material remains inert within the body, and with the newly formed tissue, augments or shapes the soft tissue as desired.

The composition of the implant material determines the nature of the tissue formation. Generally, vascularization is undesirable with soft tissue augmentation. Therefore, the particles are preferably about 500 microns in diameter or less, preferably about 50 to about 200 microns. Larger particle sizes may result in interstices between particles that are large enough to allow unwanted vascularization. In addition, growth of tissue into the implant material is dependent upon the presence and size of pores in the particles. Ingrowth helps integrate and retain the implant material in place. Preferably, the proportion of pores in the material is from about 0 percent to about 60 percent, with pore sizes of less than about 100 microns. This allows sufficient retention of the material while maintaining a high proportion of augmenting particles. Most preferably, the proportion is from about 40 to about 60 percent, and pore sizes between

about 50 and about 100 microns.

Preferred procedures for producing the polymeric particles for implant materials of the invention are disclosed in U.S. Pat. Nos. 4,535,485 and 4,547,390, the specifications of which are incorporated herein by reference. In various embodiments of the present invention, the particles may be of about 34 mesh size or smaller (particle diameters of about 500 microns or less). For embodiments of the invention containing calcium hydroxide, preferred procedures for producing polymeric particles are disclosed in U.S. Pat. No. 4,728,570, which is incorporated herein by reference.

Combining the particulate material with the matrix material may be accomplished by various methods, depending on the application. In applications where the implant site will be exposed, for example, the particulate material and matrix material may be combined into a paste. In embodiments where the implant material is to be injected, the particulate material may be placed in a syringe and the matrix material drawn into the syringe to "hydrate" the material. Those skilled in the art will appreciate these and other methods of preparing the implant material.

The present invention also contemplates a method of soft tissue augmentation. Soft-tissue implant materials of the invention are inexpensive to manufacture and may be used to advantage in many medical, dental, cosmetic, and veterinary applications. The material may be implanted into specific tissues in the body to provide desired augmentation. Preferably, the material is combined with one or more matrix materials before implantation. Preferred matrix materials are sterile water, saline solution, collagen, blood and glucose. In order for there to be ample fluidity, the matrix material may comprise a volume of between about 30% and about

65%, and most preferredly about 50%, of the implanted material. Those versed in the art will appreciate which and how much matrix material to use for a particular application.

In certain embodiments of the invention, the implant material is injected, e.g., by syringe or orthoscopic devices. These methods are preferred because they are less invasive than other, e.g., surgical, procedures, lessen the risk of infection, discomfort, and complications, and can be easily controlled in amount and location. For materials containing collagen, it is preferable that the collagen be in injectable form. One skilled in the art will know the various methods of injection. For example, embodiments of the invention having a particle size of about 500 microns may be injected using an 18-gauge syringe. Those embodiments having smaller particles may be injected with higher-gauge needles, e.g., orthoscopically.

In one embodiment of the invention, the implant material is injected subcutaneously into an area having a soft tissue contour defect. The amount implanted is in a sufficient amount to at least partially, preferably entirely, remove the defect. Such defect may include, for example, wrinkles.

Referring to the drawings, and initially to **FIG. 1**, skin **10** consists of the epidermis **11** and the dermis **12**. The hypodermis **13**, also called the subcutaneous layer, contains collagen, elastic tissue, and adipose (fat) (not shown in any more detail). The hypodermis **13** provides underlying structure for the skin, and thus greatly contributes locally to its contour **14**. The hypodermis **13** may lose its adipose, collagen, and elastic tissue, especially as the skin **10** ages. This can result in vacuities **15** in the hypodermis and loss of support for the overlaying dermis **12** and epidermis **11**, i.e., the skin sags, forming wrinkles **16**.

In **FIG. 2**, the implant material **20** of the present invention has been injected under the skin **10** into the hypodermis **13** beneath the dermis **12**. The implant material **20** fills the vacuities **15**, providing support for the skin **10**. The material **20** also pushes out the skin **10**, causing it to have a much smoother surface contour **21**.

In another embodiment of the invention, the implant material may be used to control incontinence. Such incontinence may be the result of disease, aging, or neuromuscular degeneration. It may also result from prostate surgery that causes localized damage to the nerves controlling the sphincter surrounding the urethra. As shown in **FIG. 3**, the urethra **30** is connected to the bladder **31**. The sphincter urethrae **32** is attached to the pelvis **33** and surrounds the urethra **30**. The prostate **34** (shown in phantom) which surrounds the urethra **30** between the bladder **31** and the sphincter urethrae **32** is shown as having been previously removed surgically. Often this surgery damages the controlling sphincter urethrae **32** or causes indirect flaccidity due to nerve damage. Where a patient has lost some or all control of the sphincter urethrae **32**, he will not be able to constrict the urethra **30** and prevent urine flow. In the present invention, implant material **35** is injected into the sphincter urethrae **32**, swelling it, reshaping it, and causing at least a partial closure and constriction **36** of the urethra **30**. Contraction of other muscles, e.g., the abdominal muscles, in the area of the bladder (not shown) will push the sphincter **32** and allow urine to flow past the constriction **36**, even where there is no direct control over the sphincter.

Preferably, between about 2cc and about 4cc of implant material is injected into the sphincter urethrae **32** to cause constriction **36** of the urethra **30**. However, one skilled in the art

will appreciate how much implant material to inject according to the particular medical condition of the patient.

Those skilled in the art will recognize that the compositions and methods of the present invention will have various other uses in addition to the above described embodiments. They will appreciate that the foregoing specification and accompanying drawings are set forth by way of illustration and not limitation of the invention. It will further be appreciated that various modifications and changes may be made therein without departing from the spirit and scope of the present invention, which is to be limited solely by the scope of the appended claims.

What is claimed is:

1. A soft tissue implant material comprising biologically-compatible polymeric particles having intraparticulate pores, said pores having dimensions effective to permit soft tissue to grow therein.

2. Implant material of claim 1 wherein said particles have a diameter of up to about 500 microns.

3. Implant material of claim 2 wherein said particles have a diameter of about 50 to about 200 microns.

4. Implant material of claim 1 wherein said particles have interstices therebetween, said interstices having dimensions effective to permit soft tissue to grow therein.

5. Implant material of claim 1 wherein said pores comprise between about zero and about 60 percent of said implant material.

6. Implant material of claim 5 wherein said pores comprise between about 40 and about 60 percent of said implant material.

7. Implant material of claim 1 wherein said pores have a size of less than about 100 microns.

8. Implant material of claim 7 wherein said pores have a size of between about 50 and about 100 microns.

9. Implant material of claim 1 further comprising collagen.

10. Implant material of claim 9 wherein said collagen comprises between about 30% and about 65% of said implant material by volume.

11. Implant material of claim 10 wherein said collagen comprises about 50% of said implant material by volume.

12. Implant material of claim 9 wherein said collagen comprises injectable collagen.

13. Implant material of claim 1 wherein said particles have an inner core comprised of a first biologically-compatible polymeric material and an outer layer generally surrounding said inner core, said outer coating comprised of a second biologically-compatible polymeric material, said second polymeric material being hydrophilic and having a composition different from the composition of said first polymeric material.

14. Implant material of claim 13 wherein said first polymeric material is an acrylic polymer.

15. Implant material of claim 14 wherein said first polymeric material is polymethylmethacrylate.

16. Implant material of claim 13 wherein said second polymeric material is a polymeric hydroxyethylmethacrylate.

17. Implant material of claim 16 wherein said polymeric hydroxyethylmethacrylate comprises a copolymer of monomeric hydroxyethylmethacrylate and a cross-linking agent.

18. Implant material of claim 1 further comprising at least one bioactive substance.

19. Implant material of claim 18 wherein said at least one bioactive substance is grafted to said biologically-compatible particles.

20. Implant material of claim 13 further comprising a coating of calcium hydroxide on said outer layer.

21. A method of augmenting soft tissue comprising:

a. providing a biologically-compatible implant material comprised of biologically compatible polymeric particles; and

b. implanting said implant material within soft tissue.

22. Method of claim 21 wherein said implanting step includes the step of injecting said implant material.

23. Method of claim 22 wherein said injecting step includes injecting said implant material subcutaneously into an area having a soft tissue contour defect in an amount sufficient to at least partially remove said defect.

24. Method of claim 23 wherein said soft tissue contour defect comprises wrinkles.

25. Method of claim 23 wherein said soft tissue contour defect includes gingival soft tissue defects in the mouth.

26. Method of claim 22 wherein said injecting step includes injecting said material into the sphincter surrounding the urethra in an amount sufficient to at least partially constrict said urethra.

27. Method of claim 26 wherein said injecting step includes injecting between about 2 cc and about 4 cc of said implant material.

28. Method of claim 21 wherein said particles have a diameter of up to about 500 microns.

29. Method of claim 28 wherein said particles have a diameter of about 50 to about 200 microns.

30. Method of claim 21 wherein said particles have intraparticulate pores, said pores having dimensions effective to permit soft tissue to grow therein.

31. Method of claim 30 wherein said pores comprise between about zero and about 60 percent of said material.

32. Method of claim 31 wherein said pores comprise between about 40 and about 60 percent of said material.

33. Method of claim 30 wherein said pores have a size of less than about 100 microns.

34. Method of claim 33 wherein said pores have a size of between about 50 and about 100 microns.

35. Method of claim 21 wherein said particles have interstices therebetween, said interstices having dimensions effective to permit soft tissue to grow therein.

36. Method of claim 21 wherein said particles have an inner core comprised of a first biologically-compatible polymeric material and an outer layer generally surrounding said inner core, said outer coating comprised of a second biologically-compatible polymeric material, said second polymeric material being hydrophilic and having a composition different from the composition of said first polymeric material.

37. Method of claim 36 further comprising a coating of calcium hydroxide on said outer layer.

38. Method of claim 36 wherein said first polymeric material is an acrylic polymer.

39. Method of claim 38 wherein said first polymeric material is polymethylmethacrylate.

40. Method of claim 36 wherein said second polymeric material is a polymeric hydroxyethylmethacrylate.

41. Implant material of claim 40 wherein said polymeric hydroxyethylmethacrylate comprises a copolymer of monomeric hydroxyethylmethacrylate and a cross-linking agent.

42. Method of claim 21 wherein the step of providing a biologically compatible implant material further comprises combining said particles with a matrix material.

43. Method of claim 42 wherein said matrix material comprises a volume of between about 30% and about 65% of the volume of said implant material.

44. Method of claim 43 wherein said matrix material comprises a volume of about 50% of the volume of said implant material.

45. Method of claim 42 wherein said matrix material is selected from the group consisting of sterile water, saline solution, adipose tissue, blood, glucose, hyaluronic acid, and collagen.

46. Method of claim 45 wherein said matrix material comprises collagen.

47. Method of claim 46 wherein said collagen comprises injectable collagen.

48. Method of claim 21 wherein the step of providing a biologically compatible implant material further comprises the step of combining said particles with at least one bioactive substance.

49. Method of claim 48 wherein the combining step includes grafting said at least one bioactive substance to said particles.

ABSTRACT OF THE DISCLOSURE

A soft tissue implant material is formed from biologically-compatible polymeric particles. The particles may have a diameter of up to about 500 microns and intraparticulate pores sized for ingrowth of soft tissue. The particles may have an inner core of a first biologically-compatible polymeric material and an outer layer generally surrounding the inner core, with the outer layer comprised of a second biologically-compatible polymeric material being hydrophilic and having a composition different from the composition of the first polymeric material. The material may be utilized with collagen or other matrix materials. This material may be used in a method of reforming soft tissues by implanting the material within soft body tissues to modify soft tissue defects such as wrinkles or oral gingival tissue defects and reshape soft tissue, e.g., for urinary bladder inconvenience.

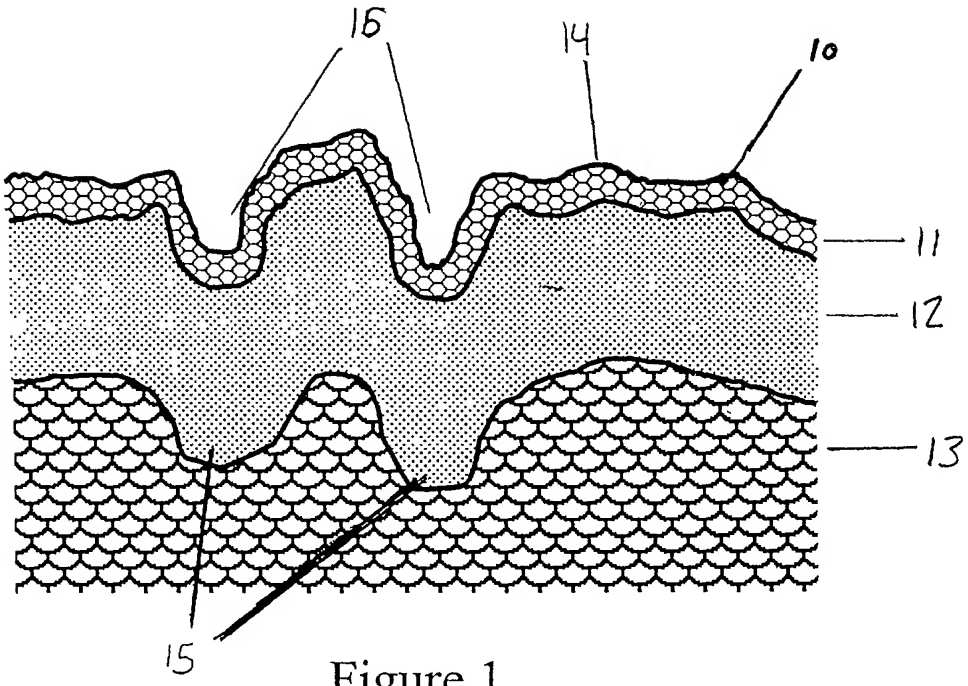

Figure 1

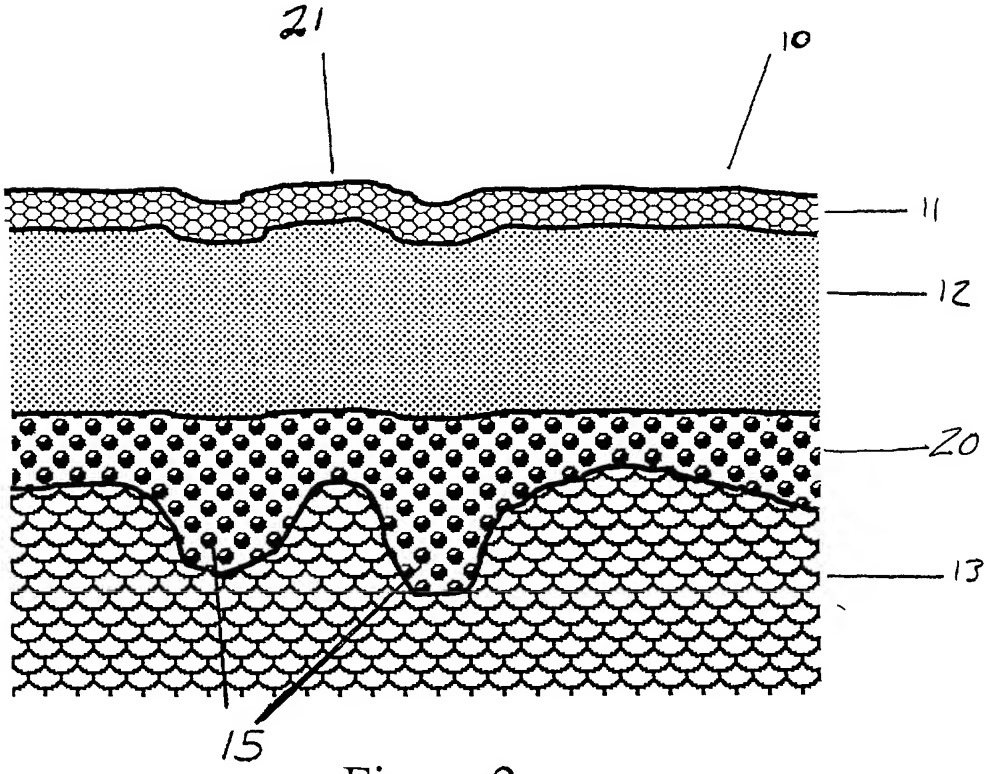

Figure 2

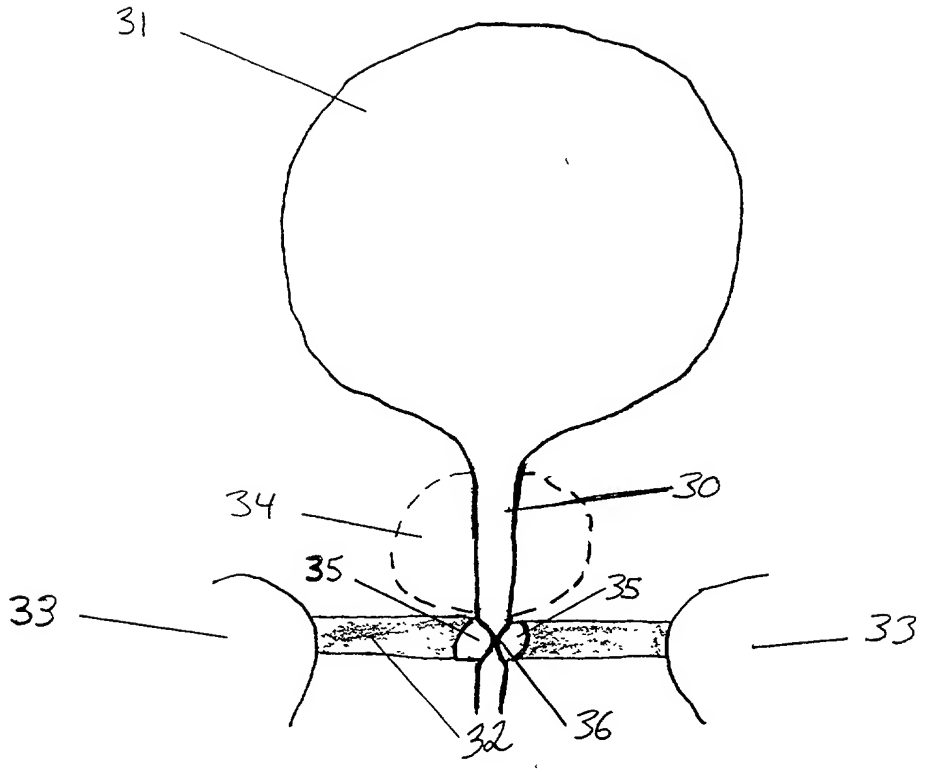

Figure 3

Docket No.: 1527/0E847

DECLARATION
AND POWER OF ATTORNEY

As a below named inventor, I declare that the information given herein is true, that I believe that I am the original, first and sole inventor if only one name is listed at 1 below, or a joint inventor if plural inventors are named below, of the invention entitled:

SOFT TISSUE SUBSTITUTE AND METHOD OF SOFT TISSUE REFORMATION

which is described and claimed in:

[X] the attached specification or [] the specification in application Serial No. , filed
(for declaration not accompanying appl.)

that I do not know and do not believe that the same was ever known or used in the United States of America before my or our invention thereof or patented or described in any printed publication in any country before my or our invention thereof, or more than one year prior to this application, or in public use or on sale in the United States of America more than one year prior to this application, that the invention has not been patented or made the subject of an inventor's certificate issued before the date of this application in any country foreign to the United States of America on an application filed by me or my legal representatives or assigns more than twelve months prior to this application, that I acknowledge my duty to disclose information of which I am aware which is material to patentability in accordance with 37 CFR §1.56. I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I hereby claim the priority benefits under 35 U.S.C. §119 of any application(s) for patent or inventor's certificate listed below. All foreign applications for patent or inventor's certificate on this invention filed by me or my legal representatives or assigns prior to the application(s) of which priority is claimed are also identified below.

PRIOR APPLICATION(S), IF ANY, OF WHICH PRIORITY IS CLAIMED

COUNTRY	APPLICATION NO.	DATE OF FILING

ALL FOREIGN APPLICATIONS, IF ANY, FILED PRIOR TO THE APPLICATION(S) OF WHICH PRIORITY IS CLAIMED

COUNTRY	APPLICATION NO.	DATE OF FILING

POWER OF ATTORNEY:

As a named inventor, I hereby appoint the following attorney(s) and/or agents(s) to prosecute this application and transact all business in the Patent and Trademark office connected therewith: Gordon D. Coplein #19,165, William F. Dudine, Jr. #20,569, Michael J. Sweedler #19,937, S. Peter Ludwig #25,351, Paul Fields #20,298, Marc S. Gross #19,614, Harold E. Wurst #22,183, Joseph B. Lerch #26,936, Melvin C. Garner #26,272, Ethan Horwitz #27,646, Beverly B. Goodwin #28,417, Adda C. Gogoris #29,714, Martin E. Goldstein #20,869, Bert J. Lewen #19,407, Henry Sternberg #22,408, Robert A. Green #28,301, Peter C. Schechter #31,662, Robert Schaffer #31,194, David R. Francescani #25,159, Robert C. Sullivan, Jr. #30,499, Ira J. Levy #35,587, Joseph R. Robinson #33,448, Kevin Reiner #43,030

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FULL NAME AND RESIDENCE OF INVENTOR 3

LAST NAME: FIRST NAME: MIDDLE NAME:

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I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 1: _____ DATED: 11/22/99
Arthur Ashman

SIGNATURE OF INVENTOR 2: _____ DATED: _____

SIGNATURE OF INVENTOR 3: _____ DATED: _____